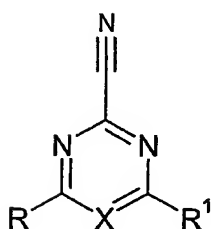


CLAIMS

1. Use use of a compound of formula (I)



(I)

10 in which:

X is N or CA where A is hydrogen, halogen, CHR^2R^3 , OR^2 , NR^2R^3 , SR^2 ;

R^2 and R^3 are independently hydrogen, C_{1-6} alkyl or C_{3-6} cycloalkyl both of which can optionally contain one or more O, S or NR^4 groups where R^4 is hydrogen or C_{1-6} alkyl, and can be optionally substituted by aryl, heteroaryl, NR^5R^6 where R^5 and R^6 together with the nitrogen atom to which they are attached form a 4-7 membered ring optionally containing a further O, S, NR^4 , or R2 and R3 together with the nitrogen atom to which they are attached form a 4-7 membered ring optionally containing a further O, S, NR^4 group, or R2 and R3 are aryl or heteroaryl groups, both aryl and heteroaryl groups being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR^7R^8 , $\text{SO}_2\text{NR}^7\text{R}^8$, SO_2R^4 , trifluoromethyl, NHSO_2R^4 , NHCOR^4 , ethylenedioxy, methylenedioxy, C_{1-6} alkyl, C_{1-6} alkoxy, NR^7R^8 or SR^7 where R^7 and R^8 are independently hydrogen or C_{1-6} alkyl;

25 R and R^1 are independently a group $\text{Y}(\text{CH}_2)_p\text{R}^9$ where p is 0, 1, 2 or 3 and Y is O or NR^{10} where R^{10} is hydrogen, C_{1-6} alkyl or C_{3-6} cycloalkyl; and R^9 is hydrogen, C_{1-6} alkyl which can optionally contain one or more O, S or NR^4 groups where R^4 is hydrogen or C_{1-6} alkyl, or a 3 to 7-membered saturated ring optionally containing a carbonyl group, one or more O, S or N atoms, or an aryl or heteroaryl group containing one to four heteroatoms selected from O, S or N, the saturated ring, aryl and heteroaryl groups all being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR^7R^8 , $\text{SO}_2\text{NR}^7\text{R}^8$, SO_2R^4 , trifluoromethyl, NHSO_2R^4 , NHCOR^4 ,

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ethylenedioxy, methylenedioxy, C₁₋₆ alkyl, C₁₋₆ alkoxy, SR⁵ or NR¹¹R¹² where R¹¹ and R¹² are independently hydrogen, C₁₋₆ alkyl or together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or NR⁴ group;

- 5 or R/R¹ is a group NR¹⁰(CHR¹⁰)CONR²R³ or NR¹⁰(CH₂)_qCONR²R³ where q is 1, 2 or 3; or R/R¹ is a group NR¹³R¹⁴ where R¹³ and R¹⁴ together with the nitrogen atom to which they are attached form a 4 to 7-membered saturated ring optionally containing a carbonyl group, O, S or N atom and optionally substituted by C₁₋₆ alkyl, amino, hydroxy, CO₂C₁₋₆ alkyl, halogen, NR⁵R⁶, NR⁷R⁸, C₁₋₆ alkylNR¹⁷R¹⁸ where R¹⁷ and R¹⁸ are independently
10 hydrogen or C₁₋₆ alkyl, CONR¹⁵R¹⁶ where R¹⁵ and R¹⁶ are independently hydrogen or C₁₋₆ alkyl, or optionally substituted by aryl, phenoxy, COphenyl, or a heteroaryl group, the latter four groups being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR⁷R⁸, SO₂NR⁷R⁸, SO₂R⁴, trifluoromethyl, NHSO₂R⁴, NHCOR⁴, ethylenedioxy, methylenedioxy, C₁₋₆ alkyl, C₁₋₆ alkoxy, SR⁵ or NR¹¹R¹² where R¹¹ and R¹²
15 are independently hydrogen, C₁₋₆ alkyl or together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or NR⁴ group;

and pharmaceutically acceptable salts or solvates thereof, in the manufacture of a
20 medicament for use in the inhibition of cathepsin S in a mammal such as man.

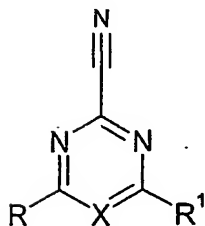
2. Use compound according to claim 1 in which X is CH, NHR², OR² where R² is hydrogen or C₁₋₆ alkyl.
- 25 3. Use compound according to claim 1 or 2 in which R is a group Y(CH₂)_pR⁷ where p is 0 or 1 and Y is NR⁸ where R⁸ is hydrogen and R⁷ is substituted phenyl.
4. Use compound according to any one of claims 1 to 3 in which R¹ is a group NR¹³R¹⁴ where R¹³ and R¹⁴ together with the nitrogen atom to which they are attached form a
30 morpholine ring, piperidine or piperazine ring optionally substituted.
5. Use compound according to any one of claims 1 to 3 in which R¹ is a group NR⁹R¹⁰ where R¹⁰ is H or C₁₋₆ alkyl and R⁹ is C₁₋₆ alkyl which can optionally contain one or more O, S or NR⁴ groups where R⁴ is hydrogen or C₁₋₆ alkyl.
- 35 6. Use according to claim 1 where the compound of formula (I) is selected from:

- 4-[(4-Chlorophenyl)amino]-6-(dimethylamino)-1,3,5-triazine-2-carbonitrile,
4-Morpholin-4-yl-6-(4-phenoxy-piperidin-1-yl)-1,3,5-triazine-2-carbonitrile,
4-[(4-Chlorophenyl)amino]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,
4-(7-Azabicyclo[2.2.1]hept-7-yl)-6-[(4-chlorophenyl)amino]-1,3,5-triazine-2-carbonitrile,
5 4-[(4-Chlorophenyl)amino]-6-pyrrolidin-1-yl-1,3,5-triazine-2-carbonitrile,
4-[(4-Chlorophenyl)amino]-6-piperidin-1-yl-1,3,5-triazine-2-carbonitrile,
4-[(4-Chlorophenyl)amino]-6-(ethylamino)-1,3,5-triazine-2-carbonitrile,
4-[(4-Chlorophenyl)amino]-6-(3-hydroxypyrrolidin-1-yl)-1,3,5-triazine-2-carbonitrile,
4-[(4-Chlorophenyl)amino]-6-[(2-piperidin-1-ylethyl)amino]-1,3,5-triazine-2-carbonitrile,
10 4-[(4-Chlorophenyl)amino]-6-(4-phenylpiperidin-1-yl)-1,3,5-triazine-2-carbonitrile,
4-[(3-Chlorobenzyl)amino]-6-(dimethylamino)-1,3,5-triazine-2-carbonitrile,
4-Morpholin-4-yl-6-[(4-morpholin-4-ylphenyl)amino]-1,3,5-triazine-2-carbonitrile,
4-(2,3-Dihydro-1,4-benzodioxin-6-ylamino)-6-morpholin-4-yl-1,3,5-triazine-2-
carbonitrile,
15 4-Morpholin-4-yl-6-(3-phenylpiperidin-1-yl)-1,3,5-triazine-2-carbonitrile,
4-(1,4'-Bipiperidin-1'-yl)-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,
4-[4-(1H-Imidazol-1-yl)piperidin-1-yl]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,
4-[4-(4-Chlorobenzoyl)piperidin-1-yl]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,
4-[4-(5-Chloropyridin-2-yl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,
20 4-Morpholin-4-yl-6-[[3-(2-oxopyrrolidin-1-yl)propyl]amino]-1,3,5-triazine-2-carbonitrile,
1-(4-Cyano-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N,N-diethylpiperidine-3-carboxamide,
4-[4-(2-Methoxyphenyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,
N~2~(4-Cyano-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N~1~,N~1~-bis{4-[N-(4-cyano-6-
morpholin-4-yl-1,3,5-triazin-2-yl)-N-isobutylglycyl]morpholin-3-yl}-N~2~-
isobutylglycinamide,
25 4-Morpholin-4-yl-6-[(2-pyridin-3-ylethyl)amino]-1,3,5-triazine-2-carbonitrile,
4-[[2-(2-Furyl)ethyl]amino]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,
4-[(4-Chlorophenyl)amino]-6-(4-methylpiperazin-1-yl)-1,3,5-triazine-2-carbonitrile,
4-Azetidin-1-yl-6-[(4-chlorophenyl)amino]-1,3,5-triazine-2-carbonitrile,
30 4-[(4-Chlorophenyl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,
4-[(4-Methylcyclohexyl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,
4-(4-Chlorophenoxy)-6-morpholin-4-ylpyrimidine-2-carbonitrile,
4-[(4-Chlorophenyl)amino]-6-(dimethylamino)pyrimidine-2-carbonitrile,
4-[(1-Methylpiperidin-4-yl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,
35 4-(Cyclohexylamino)-6-morpholin-4-ylpyrimidine-2-carbonitrile,
4-[(4-Chlorophenyl)amino]-6-pyrrolidin-1-ylpyrimidine-2-carbonitrile,

4-[(6-Chloropyridin-3-yl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,
 1-{6-[(4-Chlorophenyl)amino]-2-cyanopyrimidin-4-yl}-L-prolinamide,
 4-(4-Aminopiperidin-1-yl)-6-[(4-chlorophenyl)amino]pyrimidine-2-carbonitrile,
 4-[(4-Chlorophenyl)amino]-6-(4-pyrrolidin-1-ylpiperidin-1-yl)pyrimidine-2-carbonitrile,
 5 4-[(4-Chlorophenyl)amino]-6-[(3-pyrrolidin-1-ylpropyl)amino]pyrimidine-2-carbonitrile,
 tert-Butyl 4-{6-[(4-chlorophenyl)amino]-2-cyanopyrimidin-4-yl}piperazine-1-carboxylate,
 4-[(4-Chlorophenyl)amino]-6-(cyclopropylamino)pyrimidine-2-carbonitrile,
 4-[(4-Chlorophenyl)amino]-6-piperazin-1-ylpyrimidine-2-carbonitrile,
 (2S)-N~2~-{6-[(4-Chlorophenyl)amino]-2-cyanopyrimidin-4-yl}-N~1~,N~1~-bis[4-(N-
 10 {6-[(4-chlorophenyl)amino]-2-cyanopyrimidin-4-yl}-L-leucyl)morpholin-3-yl]-L-
 leucinamide,
 5-Chloro-4-[(4-chlorophenyl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,
 4-[(4-Chlorophenyl)amino]-5-methoxy-6-piperazin-1-ylpyrimidine-2-carbonitrile,
 4-[(4-Chlorophenyl)amino]-5-methoxy-6-morpholin-4-ylpyrimidine-2-carbonitrile,
 15 4-[(3S)-3-Aminopyrrolidin-1-yl]-6-[(4-chlorophenyl)amino]-5-methoxypyrimidine-2-
 carbonitrile,
 4-[(4-Chlorophenyl)amino]-6-{4-[3-(dimethylamino)propyl]piperazin-1-yl}-5-
 methoxypyrimidine-2-carbonitrile,
 4-[(4-Chlorophenyl)amino]-6-(dimethylamino)-5-methoxypyrimidine-2-carbonitrile,
 20 4-[(4-Chlorophenyl)amino]-5-methoxy-6-(3-oxopiperazin-1-yl)pyrimidine-2-carbonitrile,
 1-{6-[(4-Chlorophenyl)amino]-2-cyano-5-methoxypyrimidin-4-yl}piperidine-3-
 carboxamide,
 4-(4-Aminopiperidin-1-yl)-6-[(4-chlorophenyl)amino]-5-methoxypyrimidine-2-
 carbonitrile,
 25 5-Amino-4-[(4-chlorophenyl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,
 5-Amino-4-[(4-Chlorophenyl)amino]-6-(ethylamino)pyrimidine-2-carbonitrile,
 and pharmaceutically acceptable salts thereof.

7. A compound of formula (I):

30



(I)

in which:

- 5 X is CA where A is hydrogen, halogen, CHR^2R^3 , OR^2 , NR^2R^3 , SR^2 ;

R^2 and R^3 are independently hydrogen, C_{1-6} alkyl or C_{3-6} cycloalkyl both of which can optionally contain one or more O, S or NR^4 groups where R^4 is hydrogen or C_{1-6} alkyl, and
 10 can be optionally substituted by aryl, heteroaryl, NR^5R^6 where R^5 and R^6 together with the nitrogen atom to which they are attached form a 4-7 membered ring optionally containing a further O, S, NR^4 , or R^2 and R^3 together with the nitrogen atom to which they are attached form a 4-7 membered ring optionally containing a further O, S, NR^4 group, or R^2 and R^3 are aryl or heteroaryl groups, both aryl and heteroaryl groups being optionally substituted
 15 by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR^7R^8 , $\text{SO}_2\text{NR}^7\text{R}^8$, SO_2R^4 , trifluoromethyl, NHSO_2R^4 , NHCOR^4 , ethylenedioxy, methylenedioxy, C_{1-6} alkyl, C_{1-6} alkoxy, NR^7R^8 or SR^7 where R^7 and R^8 are independently hydrogen or C_{1-6} alkyl;

R and R^1 are independently a group $\text{Y}(\text{CH}_2)_p\text{R}^9$ where p is 0, 1, 2 or 3 and Y is O or NR^{10}
 20 where R^{10} is hydrogen, C_{1-6} alkyl or C_{3-6} cycloalkyl;
 and R^9 is hydrogen, C_{1-6} alkyl which can optionally contain one or more O, S or NR^4 groups where R^4 is hydrogen or C_{1-6} alkyl, or a 3 to 7-membered saturated ring optionally containing a carbonyl group, one or more O, S or N atoms, or an aryl or heteroaryl group containing one to four heteroatoms selected from O, S or N, the saturated ring, aryl and
 25 heteroaryl groups all being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR^7R^8 , $\text{SO}_2\text{NR}^7\text{R}^8$, SO_2R^4 , trifluoromethyl, NHSO_2R^4 , NHCOR^4 , ethylenedioxy, methylenedioxy, C_{1-6} alkyl, C_{1-6} alkoxy, SR^5 or $\text{NR}^{11}\text{R}^{12}$ where R^{11} and R^{12} are independently hydrogen, C_{1-6} alkyl or together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or
 30 NR^4 group;

or R/R^1 is a group $\text{NR}^{10}(\text{CHR}^{10})\text{CONR}^2\text{R}^3$ or $\text{NR}^{10}(\text{CH}_2)_q\text{CONR}^2\text{R}^3$ where q is 1, 2 or 3;
 or R/R^1 is a group $\text{NR}^{13}\text{R}^{14}$ where R^{13} and R^{14} together with the nitrogen atom to which they are attached form a 4 to 7-membered saturated ring optionally containing a carbonyl group, O, S or N atom and optionally substituted by C_{1-6} alkyl, amino, hydroxy, $\text{CO}_2\text{C}_{1-6}$
 35 alkyl, halogen, NR^5R^6 , NR^7R^8 , C_{1-6} alkyl $\text{NR}^{17}\text{R}^{18}$ where R^{17} and R^{18} are independently hydrogen or C_{1-6} alkyl, $\text{CONR}^{15}\text{R}^{16}$ where R^{15} and R^{16} are independently hydrogen or C_{1-6}

alkyl, or optionally substituted by aryl, phenoxy, COphenyl, or a heteroaryl group, the latter four groups being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR^7R^8 , $\text{SO}_2\text{NR}^7\text{R}^8$, SO_2R^4 , trifluoromethyl, NHSO_2R^4 , NHCOR^4 , ethylenedioxy, methylenedioxy, C_{1-6} alkyl, C_{1-6} alkoxy, SR^5 or $\text{NR}^{11}\text{R}^{12}$ where R^{11} and R^{12} are independently hydrogen, C_{1-6} alkyl or together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or NR^4 group;

and pharmaceutically acceptable salts or solvates thereof..

10

8. A compound of formula (I) as defined in claim 7 for use in therapy.

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9. A pharmaceutical composition which comprises a compound of the formula (I) as defined in claim 7 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable diluent or carrier.

20

10. A method for producing inhibition of a cysteine protease in a mammal, such as man, in need of such treatment, which comprises administering to said mammal an effective amount of a compound of the present invention as defined in claim 7 or a pharmaceutically acceptable salt thereof.